Remarks

Claims 32 and 34-50 are pending. Claim 34 has been amended. Claim 45 has been canceled. Claim 34 was amended to more clearly claim what applicants consider to be their invention.

Claim 34 was amended to incorporate a limitation of previously presented claim 45 (wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence).

Applicants also acknowledge that Claims 32 and 35-38 have been allowed and thank the Examiner for indicating as much.

Rejection Under 35 U.S.C. § 102

1. Claims 34 and 39-45 were rejected under 35 U.S.C. § 102(b), as being anticipated by Hartley (5,043,272). Applicants respectfully traverse this rejection to the extent it applies to the claims as amended.

Hartley et al. discloses a process for the amplification of a nucleic acid template in a sample, which process comprises synthesis of nucleic acid sequences in a randomly primed, but template dependent manner. The method, described as Random Priming Amplification (RPA) employs the use of random primers (see Hartley et al. column 2, lines 54 – column 3, line 2). The primers disclosed by Hartley et al. contain sequences not designed to be directed to a specific sequence in the nucleic acid sample to be amplified (see Hartley et al. column 5, lines 14).

The passages of Hartley et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence.

Claims 34 and 39-45 that depend from Claim 34, are drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial

complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require that the primers have random nucleotide sequences. In addition to the random nucleotide sequences, the primers comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. In other words, within the set of primers in the kit, each primer has a constant portion that is the same as each and every other primer in the set. (see Amended Claim 34 above, lines 5-7).

The Office Action alleges (page 2, lines 16-17) that Hartley et al. teaches "the constant portion of the primer has the same nucleotide sequence." For support, the Office Action cites column 12, lines 16-22, which describes the HPV Capture Oligonucleotide Sequence (column 12, lines 10-22). In other words, the Office Action alleges that the HPV Capture Oligonucleotide Sequence is a constant portion of the random primers described by Hartley et al. This is simply incorrect. The HPV Capture Oligonucleotide Sequence is not a primer. The HPV Capture Oligonucleotide Sequence is exactly what its name states, it is a capture oligonucleotide used by Hartley et al. to immobilize the HPV target sequence. Nowhere in Hartley et al. is the HPV Capture Oligonucleotide Sequence or any Capture Oligonucleotide Sequence used as a primer. In fact, Hartley et al. specifically teaches away from such a possibility as evidenced in column 12, lines 25-29, where the random primers described by Hartley et al. are added after the HPV target has been immobilized and excess reagents washed away. Even if the HPV Capture Oligonucleotide Sequence was used as a primer, which it is not, all that is disclosed in the portion of Hartley et al. cited by the Examiner is a single nucleic acid sequence. Nowhere is there any description that the HPV Capture Oligonucleotide Sequence is random, nor is there any description that the portions of the HPV Capture Oligonucleotide Sequence is constant between all HPV Capture Oligonucleotide Sequences.

The cited passage of Hartley et al. fails to disclose a kit for amplifying a target nucleic acid sequence, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. Because Hartley et al. fails to disclose every feature of the claimed kits, Hartley et al. fails to anticipate claims 34 and 39-45.

2. Claims 47-49 were rejected under 35 U.S.C. § 102(e), as being anticipated by McCaslin et al. (5,614,390). Applicants respectfully traverse this rejection.

McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers described by McCaslin et al. were designed to species-specifically amplify a target in both typical and atypical strains of *M. kansasii* (see McCaslin et al. column 3, lines 34-37).

The passages of McCaslin et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Claims 47 and 48-49 that depend from Claim 47, are drawn to a kit a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require that the each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4). In addition, the claims require that all of the

primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). Furthermore, the claims require that the set of primers has 3 or more primers (see claim 47, lines 5-6). It is important to note that each of the 3 or more primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 2, line 26 – page 3, line 2) that the teachings of McCaslin et al. anticipate the limitations of the claims. For support, the Office Action cites sections of McCaslin et al. that describe the use of primers designed for species-specific detection and identification of *Mycobacterium kansasii*. The Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of McCaslin et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, and wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Applicants submit that it would not be possible to point to such a description, as McCaslin et al. fails to teach these elements. As such, Applicants submit the Examiner has not met her burden of providing specific reference to where McCaslin et al. discloses each and every element of the claims. Because McCaslin et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

3. Claims 47 was rejected under 35 U.S.C. § 102(e), as being anticipated by Walker et al. (5,736,365). Applicants respectfully traverse this rejection.

Walker et al. discloses methods for simultaneous amplification of multiple target sequences by sequence specific hybridization of primers, particularly by SDA (multiplex SDA) (see Walker et al. column 4, lines 34-36). The methods use a single pair of amplification primers or a single SDA amplification primer to coamplify the multiple target sequences (see Walker et al. column 4, lines 36-39).

The passages of Walker et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Claim 47 is drawn to a kit a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). Furthermore, the claims require that the set of primers has 3 or more primers (see claim 47, lines 5-6). It is important to note that each of the 3 or more primers in the primer set of the kit, must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 3, lines 3-9) that the teachings of Walker et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Walker et al. that describe packaging the primers and/probes for performing adapter-mediated multiplex amplification of the IS6110 insertion element of *Mycobacterium tuberculosis* (M.tb) and the 16S ribosomal gene of *Mycobacterium tuberculosis* complexes. The Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of Walker et al. that disclose a set of primers wherein the set of primers comprises a

plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Applicants submit that it would not be possible to point to such a description, as Walker et al. fails to teach these elements. As such, Applicants submit the Examiner has not met her burden of providing specific reference to where Walker et al. discloses each and every element of the claims. Because Walker et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 103

Claims 46 and 50 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Hartley (5,043,272) as applied to claims 34 and 39-45 or over McCaslin et al. (5,614,390) as applied to claims 47-49 or over Walker et al. (5,736,365) as appied to claim 47, and further in view of Blanco et al. (Journal of Biological Chemistry, 1989, Vol. 264(15), pg. 8935-40). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

Claim 46

With regard to the subject matter of claim 46, Applicants first note that Claim 46 depends from claim 34 and by definition encompasses all the elements of Claim 34. This is important because the Office Action applies Hartley et al. in the same way and for the same disclosures for which Hartley et al. was applied in the rejection of claim 34 and 39-45 under 35 U.S.C. § 102(b) addressed above. Specifically, the Office Action alleges (page 2, lines 16-17) that Hartley et al. teaches "the constant portion of the primer has the same nucleotide sequence." For support, the Office Action cites column 12, lines 16-22, which describes the HPV Capture Oligonucleotide Sequence (column 12, lines 10-22). In other words, the Office Action alleges that the HPV Capture Oligonucleotide Sequence is a constant portion of the random primers described by Hartley et al. This is simply incorrect. The HPV Capture Oligonucleotide Sequence is not a primer. The HPV Capture Oligonucleotide Sequence is exactly what its name states, it is a capture oligonucleotide used by Hartley et al. to immobilize the HPV target sequence. Nowhere in Hartley et al. is the HPV Capture Oligonucleotide Sequence or any Capture Oligonuleotide Sequence used as a primer. In fact, Hartley et al. specifically teaches away from such a possibility as evidenced in column 12, lines 25-29, where the random primers described by Hartley et al. are added after the HPV target has been immobilized and excess reagents washed away. Even if the HPV Capture Oligonucleotide Sequence was used as a primer, which it is not, all that is disclosed in the portion of Hartley et al. cited by the Examiner is a single nucleic acid sequence. Nowhere is there any description that the HPV Capture Oligonucleotide Sequence is random, nor is there any description that the portions of the HPV Capture Oligonucleotide Sequence is constant between all HPV Capture Oligonucleotide Sequences. As discussed above, the cited passage of Hartley et al. fails to disclose a kit for amplifying a target nucleic acid sequence, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence.

Blanco et al. fails to supplement the elements missing from Hartley et al. Blanco et al. was cited for its alleged disclosure that phage vphi 29 DNA polymerase is highly processive in

the absence of any accessory protein and is able to produce strand displacement coupled to the polymerization process. Blanco et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. Thus, Hartley et al. and Blanco, either alone or in combination, fail to disclose or suggest each and every element of claim 46. Accordingly, Hartley et al. and Blanco et al. do not make obvious claim 46. Applicants respectfully request withdrawal of this rejection.

Claim 50

With regard to the subject matter of Claim 50, Applicants first note that Claim 50 depends from Claim 47 and by definition encompasses all the elements of Claim 34. This is important because the Office Action applies McCaslin et al. and Walker et al. in the same way and for the same disclosures for which McCaslin et al. and Walker et al. were applied in the rejection of claims 47-49 and 47, respectively, under 35 U.S.C. § 102(e) addressed above. Concerning McCaslin et al., Office Action alleges (page 2, line 26 – page 3, line 2) that the teachings of McCaslin et al. anticipate the limitations of the claims. For support, the Office Action cites sections of McCaslin et al. that describe the use of primers designed for species-specific detection and identification of *Mycobacterium kansasii*. The Office Action fails to specifically address each and every limitation of the claims. In particular, the Examiner has failed to address or direct the Applicants attention to portions of McCaslin et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers, which Applicants submit would not be possible, as McCaslin et al. fails to teach these elements. As described above, Applicants submit the Examiner has not met her burden of providing specific reference to where the McCaslin et al. discloses each and every element of the claims.

With respect to Walker et al., the Office Action alleges (page 3, lines 3-9) that the teachings of Walker et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Walker et al. that describe packaging the primers and/probes for performing adapter-mediated multiplex amplification of the IS6110 insertion element of *Mycobacterium tuberculosis* (M.tb) and the 16S ribosomal gene of *Mycobacterium tuberculosis* complexes. The Office Action fails to specifically address each and every limitation of the claims. In particular, the Examiner has failed to address or direct the Applicants attention to portions of Walker et al. that address a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers, which Applicants submit would not be possible, as Walker et al. fails to teach these elements. As such, Applicants submit the Examiner has not met her burden of providing specific reference to where Walker et al. discloses each and every element of the claims.

Blanco et al. fails to supplement the elements missing from McCaslin et al. and Walker et al. Blanco et al. was cited for its alleged disclosure that phage vphi 29 DNA polymerase is highly processive in the absence of any accessory protein and is able to produce strand displacement coupled to the polymerization process. The Examiner has not relied on Blanco et al. nor directed the Applicants to any portions of Blanco et al. that address a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers, which Applicants submit would not be possible, as Blanco et al. fails to teach these elements.

As such, Applicants submit the Examiner has not met her burden of providing specific reference to where either McCaslin et al., Walker et al. or Blanco et al. either alone or in combination disclose or suggest each and every element of the claims. Furthermore, Applicants

submit that McCaslin et al., Walker et al. and Blanco, either alone or in combination, fail to disclose or suggest each and every element of claim 46. Accordingly, Hartley et al. and Blanco et al. do not make obvious claim 50. Applicants respectfully request withdrawal of this rejection.

Respectfully submitted,

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